

Applicants : Michael Wayne Graham and Robert Norman Rice
Serial No. : 10/646,070
Filed : August 22, 2003
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Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

1-47. (Canceled)

48. (Currently Amended) A double-stranded synthetic DNA gene, comprising multiple copies of a structural gene region, wherein the structural gene region comprises a nucleotide sequence which consists of greater than 20 consecutive nucleotides and which is identical to a nucleotide sequence of a target gene in a ~~vertebrate animal~~ eukaryotic cell,

wherein one of the copies is placed in the sense orientation and another of the copies is placed in the antisense orientation operably under the control of a single promoter sequence which is operable in the cell,

~~and~~ wherein the copy of the structural gene region placed in the sense orientation and the copy of the structural gene region placed in the antisense orientation are arranged so as to form an interrupted palindrome sequence which is operably under the control of the single promoter sequence-, and

wherein the structural gene region placed in the sense orientation and the structural gene region placed in the antisense orientation are separated by a sequence of nucleotides that is 50-100 nucleotides in length or 100-500 nucleotides in length.

49-109. (Canceled)

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110. (Currently Amended) A double-stranded DNA construct, comprising a synthetic DNA gene and a genetic sequence which provides for the maintenance and/or replication of the double-stranded DNA ~~synthetic genetic~~ construct in prokaryotes or eukaryotes and/or the integration of the double-stranded DNA construct or a part thereof into the genome of a eukaryotic cell or organism,

wherein the synthetic DNA gene comprises multiple copies of a structural gene region,

wherein the structural gene region comprises a nucleotide sequence which consists of greater than 20 consecutive nucleotides and which is identical to a nucleotide sequence of a target gene in a ~~vertebrate animal~~ eukaryotic cell,

wherein one of the copies is placed in the sense orientation and another of the copies is placed in the antisense orientation operably under the control of a single promoter sequence which is operable in the cell,

~~and~~ wherein the copy of the structural gene region placed in the sense orientation and the copy of the structural gene region placed in the antisense orientation are arranged so as to form an interrupted palindrome sequence which is operably under the control of the single promoter sequence-, and

wherein the structural gene region placed in the sense orientation and the structural gene region placed in the antisense orientation are separated by a sequence of nucleotides that is 50-100 nucleotides in length or 100-500 nucleotides in length.

111-113. (Canceled)

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114. (Previously Presented) The double-stranded DNA construct of claim 110, wherein the genetic sequence comprises one or more origins of replication and/or selectable marker gene sequences.
115. (Previously Presented) The double-stranded DNA construct of claim 110, which is encapsulated in a liposome.
116. (Previously Presented) The double-stranded DNA construct of claim 110, which is in a virus particle.
117. (Previously Presented) The double-stranded DNA construct of claim 116, wherein the virus particle is an attenuated virus or associated with a virus coat.
118. (Previously Presented) The double-stranded DNA construct of claim 110, which is in a recombinant viral vector.
119. (Currently Amended) The double-stranded DNA construct of claim 118, wherein the recombinant viral vector is a retrovirus ~~or a lentivirus~~.
120. (Currently Amended) The double-stranded ~~DNA~~-synthetic DNA gene of claim 48, wherein the target gene is from a viral pathogen of ~~the~~a vertebrate animal cell.
121. (Currently Amended) The double-stranded DNA construct of claim 110, wherein the target gene is from a viral pathogen of ~~the~~a vertebrate animal cell.

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122. (Previously Presented) The double-stranded synthetic DNA gene of claim 48, wherein the promoter is selected from the group consisting of an SV40 late promoter, an SV40 early promoter, an RSV-LTR promoter and a CMV IE promoter.
123. (Previously Presented) The double-stranded DNA construct of claim 110, wherein the promoter is selected from the group consisting of an SV40 late promoter, an SV40 early promoter, an RSV-LTR promoter and a CMV IE promoter.
124. (Previously Presented) The double-stranded synthetic DNA gene according to claim 48, wherein the nucleotide sequence of the target gene encodes an amino acid sequence.
125. (Previously Presented) The double-stranded DNA construct of claim 110, wherein the nucleotide sequence of the target gene encodes an amino acid sequence.
126. (Currently Amended) The double-stranded ~~DNA~~ synthetic DNA gene of claim 48, wherein the nucleotide sequence of the target gene is not capable of being translated.~~does not encode an amino acid sequence.~~
127. (Currently Amended) The double-stranded DNA construct of claim 110, wherein the nucleotide sequence of the target is not capable of being translated.~~gene does not encode an amino acid sequence.~~
128. (Currently Amended) The double-stranded synthetic DNA gene of claim 48, wherein the target gene is derived from the genome of a pathogen of the ~~vertebrate animal~~ eukaryotic cell.

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129. (Currently Amended) The double-stranded DNA construct of claim 110, wherein the target gene is derived from the genome of a pathogen of the ~~vertebrate animal~~eukaryotic cell.
130. (Currently Amended) The double-stranded synthetic DNA gene of claim 48, wherein the target gene is endogenous to the genome of the ~~vertebrate animal~~eukaryotic cell.
131. (Currently Amended) The double-stranded DNA construct of claim 110, wherein the target gene is endogenous to the genome of the ~~vertebrate animal~~eukaryotic cell.
132. (Previously Presented) A composition comprising the double-stranded DNA construct of claim 110 and a carrier, excipient or diluent suitable for human application.

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133. (Currently Amended) A ~~vertebrate animal~~ eukaryotic cell in cell or tissue culture, comprising a double-stranded synthetic DNA gene which comprises multiple copies of a structural gene region,

wherein the structural gene region comprises a nucleotide sequence which consists of greater than 20 consecutive nucleotides and which is identical to a nucleotide sequence of a target gene in the cell,

wherein one of the copies is placed in the sense orientation and another of the copies is placed in the antisense orientation operably under the control of a single promoter sequence which is operable in the cell,

~~and~~ wherein the copy of the structural gene region placed in the sense orientation and the copy of the structural gene region placed in the antisense orientation are arranged in the structural region so as to form an interrupted palindrome sequence which is operably under the control of the single promoter sequence, and

wherein the structural gene region placed in the sense orientation and the structural gene region placed in the antisense orientation are separated by a sequence of nucleotides that is 50-100 nucleotides in length or 100-500 nucleotides in length.

134. (Currently Amended) The ~~vertebrate animal~~ eukaryotic cell of claim 133, wherein the structural gene region is transcribed in the cell.

135. (Currently Amended) The ~~vertebrate animal~~ eukaryotic cell of claim 133, wherein the cell has a reduced level of expression of the target gene.

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136-138. (Canceled)

139. (Withdrawn; Currently Amended) A process of modifying a ~~vertebrate animal~~eukaryotic cell in cell or tissue culture, comprising the step of introducing the double-stranded synthetic DNA gene of claim 48 into the cell.

140. (Withdrawn; Currently Amended) A process of modifying a ~~vertebrate animal~~eukaryotic cell in cell or tissue culture comprising the step of introducing the double-stranded DNA construct of claim 110 into the cell.

141-144. (Canceled)

145. (Withdrawn; Currently Amended) A process of modifying a ~~vertebrate animal~~eukaryotic cell, comprising contacting the cell with the composition of claim 132.

146. (Currently Amended) The double-stranded synthetic DNA gene of claim 48, wherein the eukaryotic cell is a human cell.

147. (Currently Amended) The double-stranded DNA construct of claim 110, wherein the eukaryotic cell is a human cell.

148. (Currently Amended) The eukaryotic cell of claim 133, which is a human cell.

149. (Currently Amended) The eukaryotic cell of claim 133, which is an embryonic stem cell, cultured skin fibroblast, neuronal cell, somatic cell, hematopoietic stem cell or T-cell.

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150. (Withdrawn; Currently Amended) A process for selecting an appropriate nucleotide sequence for repressing, delaying or otherwise reducing expression of a target gene in a eukaryotic cell, comprising the steps of obtaining the double-stranded synthetic DNA gene of claim 48, introducing the double-stranded synthetic DNA gene into the eukaryotic cell, and assaying the eukaryotic cell for efficacy of the double-stranded synthetic DNA gene in repressing, delaying or otherwise reducing target gene expression, thereby selecting an appropriate nucleotide sequence for repressing, delaying or otherwise reducing expression of a target gene in the eukaryotic cell.
151. (Withdrawn; Previously Presented) The process of claim 150, wherein the double-stranded synthetic DNA gene is comprised in a set of diverse double-stranded synthetic DNA genes each according to claim 48, wherein each member of the set is contained within a plasmid, cosmid, bacteriophage or virus vector molecule which is suitable for maintenance and/or replication in a cellular host.
152. (Withdrawn; Currently Amended) A process for identifying the function of a target gene in specifying a phenotype in a eukaryotic cell, comprising the steps of obtaining the double-stranded synthetic DNA gene of claim 48, introducing the double-stranded synthetic DNA gene into the eukaryotic cell, and assaying the eukaryotic cell for a phenotype, thereby identifying the function of a target gene in specifying a phenotype in the eukaryotic cell.